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## ECCO essential requirements for quality cancer care: Melanoma

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### ABSTRACT

**Background:** ECCO essential requirements for quality cancer care (ERQCC) are explanations and descriptions of challenges, organisation and actions that are necessary to give high-quality care to patients who have a specific type of cancer. They are written by European experts representing all disciplines involved in cancer care.

ERQCC papers give oncology teams, patients, policymakers and managers an overview of the elements needed in any healthcare system to provide high quality of care throughout the patient journey. References are made to clinical guidelines and other resources where appropriate, and the focus is on care in Europe.

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Multidisciplinary  
 Organisation of care  
 Audit  
 Quality assurance  
 Patient-centred  
 Multidisciplinary team  
 Patient information  
 Health inequalities  
 Essential requirements  
 Guidelines  
 Healthcare system

#### Melanoma: essential requirements for quality care:

- Melanoma, the most-deadly skin cancer, is rising in incidence among fair-skinned people in Europe. Increasing complexity of care for advanced disease in clinical areas such as staging and new therapies requires attention to a number of challenges and inequalities in a diverse patient group.
- Care for advanced melanoma must only be carried out in, or in collaboration with, specialist melanoma centres which have both a core multidisciplinary team and an extended team of allied professionals, and which are subject to quality and audit procedures. Access to such units is far from universal in all European countries.
- It is essential that, to meet European aspirations for high-quality comprehensive cancer control, healthcare organisations implement the requirements in this paper, paying particular attention to multidisciplinary and patient-centred pathways from diagnosis to treatment and follow-up, to improve survival and quality of life for patients.

**Conclusion:** Taken together, the information presented in this paper provides a comprehensive description of the essential requirements for establishing a high-quality service for melanoma. The ERQCC expert group is aware that it is not possible to propose a ‘one size fits all’ system for all countries, but urges that access to multidisciplinary teams and specialised treatments is guaranteed to all patients with melanoma.

## 1. Introduction: why we need quality frameworks

There has been a growing emphasis on driving up quality in cancer organisations, given that there is wide agreement that much care is not comprehensively accessible, not well coordinated and not based on current evidence. This is the starting point of a report by the US Institute of Medicine (IOM) in 2013 (Levit et al., 2013), which is blunt in describing a ‘crisis in cancer care delivery’, as the growing number of older people will mean a rising number of cancer patients and numbers of survivors, while there are pressures on workforces amid rising costs of care and complexity of treatments. The European Cancer Concord (ECC), a partnership of patients, advocates and cancer professionals, has also recognised major disparities in the quality of cancer management and in the degree of funding in Europe, launching a European Cancer Patient’s Bill of Rights, a patient charter that underpins equitable access to optimal cancer control, cancer care and research for Europe’s citizens (Højgaard et al., 2017).

An assessment of the quality of cancer care in Europe was made as part of the first EU Joint Action on Cancer, the European Partnership for Action Against Cancer (EPAAC, <http://www.epaac.eu>), which reported in 2014 that there are important variations in service delivery between and within countries, with repercussions in quality of care. Factors such as waiting times and provision of optimal treatment can explain about a third of the differences in cancer survival, while cancer plans, for example a national cancer plan that promotes clinical guidelines, professional training and quality control measures, may be responsible for a quarter of the survival differences.

The EU Joint Action on Cancer Control (CANCON), which replaced EPAAC from 2014, also focused on quality of cancer care and in 2017 published the *European Guide on Quality Improvement in Comprehensive Cancer Control* (Albrecht et al., 2017). This recognises that many cancer patients are treated in general hospitals and not in comprehensive cancer centres (CCCs), and explores a model of ‘comprehensive cancer care networks’ that could reconcile expertise in existing healthcare systems given a lack of CCCs. Research also shows that care provided by multidisciplinary teams (MDTs) results in better clinical and organisational outcomes for patients (Prades et al., 2015).

Countries have been concentrating expertise for certain tumour types in such networks and in dedicated centres, or units, such as for childhood and rare cancers, and most CCCs have teams for the main cancer types. For common adult tumours, however, at the European level there has been widespread effort to establish universal, dedicated units only for breast cancer, following several European declarations that set a target of the year 2016 for care of all women and men with breast cancer to be delivered in specialist multidisciplinary centres. While this target has not been met (Cardoso et al., 2017), the view of

the ERQCC expert group is that the direction of travel is for all tumour types to adopt the principles of such dedicated care, as exemplified also by auditing standards emerging for other cancers such as colorectal.

There are disparities in melanoma burden and outcomes across Europe that stem from highly heterogeneous organisation of national health systems, and significant differences in designing and implementing national cancer control plans. To provide optimal quality care, we consider that melanoma patients must have access to the care pathways, MDTs and innovative or specialised treatments described in this document, and which are subject to the same approach to quality assurance, auditing and accreditation of a ‘unit’ that is emerging in breast cancer and other tumour types.

## 2. Melanoma: key facts and challenges

### 2.1. Key facts

#### 2.1.1. Epidemiology

- Melanoma is a malignant tumour that arises from the pigment-producing melanocytic cells located mostly in the skin, but also in the mucosae and ocular structures. In cutaneous melanoma, the main type of melanoma, there are several clinical and pathological subtypes, of which the most common is superficial spreading melanoma, which comprises about 70% of cases. Other main subtypes of cutaneous melanoma are nodular, lentigo maligna and acral lentiginous (including nail bed melanoma); there are also rare variants such as amelanotic and desmoplastic melanoma. Although it represents less than 5% of all types of skin cancer, melanoma is the most deadly, accounting for about 75% of skin cancer-related deaths. Uveal (eye) melanoma (ciliary body, iris or choroid) is the most common adult primary intraocular malignancy; conjunctival melanoma is rare. About half of mucosal melanoma begins in the head and neck region, and most of the remainder in the ano-rectal region and female genital tract. Cutaneous and ocular melanoma are very rare in children.
- The incidence of skin melanoma has increased consistently in fair-skinned people over the past 4 decades (Nikolaou and Stratigos, 2014). In 2012, it was the 7th most frequently diagnosed cancer in the European Union (EU) and accounted for 3% of all new cancers, according to the EURO CARE study (Crocetti et al., 2015). Figures from EUCAN show that in 2012, more than 100,000 new cases were registered in Europe (82,000 in EU countries), and there were about 22,000 deaths (16,000 EU), and a 5 year prevalence of about 391,000 (323,000 EU) (Ferlay et al., 2012; Bray et al., 2013). Incidence is still rising quickly in some countries – by 5% a year in

the Netherlands, for example.

- There has been a slight increase in melanoma 5-year survival from 82% in 1999–2001 to 85% in the 2000–2007 period most recently considered by the EUROCARE study, which also reports higher survival for certain tumour subtypes (e.g. lentigo melanoma), and that women have a higher survival for all subtypes. A recent paper looking at the global picture of melanoma shows that the greatest burden falls on New Zealand, Australia and Europe, and on older people and men (Karimkhani et al., 2017). Information on survival by stage has been limited for skin melanoma; a systematic literature review that included studies from 9 countries in Europe found that the reported 5 year overall survival varies: 95%–100% (stage I), 65%–92.8% (stage II), 41%–71% (stage III), and 9%–28% (stage IV), and concluded that there are large variations in stage-specific overall and recurrence-free survival by study type and by country (Svedman et al., 2016). Despite new treatments, advanced melanoma still has a poor prognosis.
- In Europe, there are pronounced differences among countries in incidence and mortality, although the quality of cancer registration varies so definitive figures are not available. Reported incidence is highest in Switzerland (25/100,000 per year), Denmark, Norway and the Netherlands, and lowest in Central Eastern European (CEE) countries including Albania, Greece and Romania (below 4/100,000 per year). While the highest mortality rate was in Norway, and the lowest in Greece, CEE countries have the largest share of deaths (35.5%) of the 4 European regions (Forsea et al., 2012). A paper that calculated mortality-to-incidence ratio (MIR) for European countries for melanoma as a proxy for the fatality rate showed it ranges between 0.09 in Switzerland and 0.44 in Latvia. The regional average MIR was the highest in CEE at 0.35; the lowest in Western Europe, at 0.13 (Forsea et al., 2014).
- Estimates for incidence of other melanoma types in Europe are: ocular, 4000 cases a year; mucosal, 1000; acral lentiginous, 5000; paediatric, 1000.

### 2.1.2. Risk factors

The main risk factors for skin melanoma are well established and include fair skin, excessive exposure to ultraviolet radiation (including the use of tanning beds) (Boniol et al., 2012), a history of sunburn, having a large number of moles or some atypical moles, and family history of melanoma. Immunosuppression is a risk factor for the development and aggressive evolution of melanoma.

### 2.1.3. Diagnosis and treatment

- The appearance of melanoma varies with thickness and subtype. Most lesions appear as irregular pigmented spots that show early the signs of ABCDE: Asymmetry, irregular Borders, variegated Colour, Diameter larger than 6 mm and Evolution, i.e. the tendency to change rapidly over weeks or months. Nodular melanoma may lack these signs and should be considered in any skin lesion that exhibits EFG: Evolution, Firmness to touch, and Growth. Lesions are usually asymptomatic but itching and bleeding can occur in melanomas with deeper thickness. A lesion that just looks different from others – an ‘ugly duckling’ – may also be a melanoma.
- The use of dermoscopy, serial photography and total body photography are helpful in detecting melanomas early. Diagnosis must be confirmed by a pathologist usually following an excisional biopsy of the entire lesion. The excisional biopsy is also needed to determine the thickness of the tumour (Breslow thickness), which is the most important prognostic factor of the primary in cutaneous melanoma. Breslow thickness, primary tumour ulceration and lymph node involvement are the main prognostic factors required to stage the tumour for outcome estimation and management decisions. Sentinel lymph node biopsy (SLNB) is recommended as a diagnostic and staging procedure for patients with melanomas thicker than 1 mm or

with additional risk factors and is the strongest prognostic marker. Staging follows the recommendations of the American Joint Committee on Cancer (Gershenwald et al., 2017).

- The standard treatment for primary cutaneous melanoma is complete surgical excision with safety margins dictated by the tumour's depth. Complete lymph node dissection (CLND) is performed for clinical (macroscopic) stage III disease on confirmation of lymph node invasion by imaging techniques and cytology/histology. Also, in patients with a tumour positive SLNB, with high tumour burden in the sentinel nodes, CLND can be considered by a shared patient-physician decision (Faries et al., 2017).
- Adjuvant therapies for stage III include interferon  $\alpha$  2b, and clinical trials of (neo)adjuvant treatment with immune- or targeted therapies have been published recently or are underway. Systemic therapies exist for unresectable metastatic disease – in recent years a range of new drugs have been introduced, including (combinations of) immunotherapies and targeted therapies, which have dramatically changed the prognosis of advanced melanoma. Radiotherapy can be used as an adjuvant treatment in stage III and to treat recurrences and metastases (such as in the bones or brain) and for palliation. Radiotherapy for primary skin melanoma should be considered in lentigo maligna, especially in older patients with extensive or unresectable disease. Various strategies such as immunotherapy and electrochemotherapy apply in selected cases to the treatment of isolated (sub)cutaneous metastases or tumours. Treatment of satellites and in-transit metastases have several treatment options including excision, CO<sub>2</sub> laser, electrochemotherapy, isolated limb perfusion and intra-lesional oncolytic virus therapy (e.g. T-VEC).

## 2.2. Challenges in melanoma care

### 2.2.1. Prevention

Given the rising incidence of melanoma in Europe there is a need for effective, consistent campaigns about risk factors, especially about excessive exposure to sunlight and the use of tanning beds, as the IARC has classified solar radiation, ultraviolet radiation and UV-emitting tanning devices as carcinogenic (International Agency for Research on Cancer (IARC), 2018). There are important differences in public awareness of melanoma risk across Europe (Forsea et al., 2013); many people still do not protect themselves or their children well against the sun and the use of tanning beds has been banned in only a few countries so far, although more have instituted bans for those under age 18. The current legal framework in the EU to regulate the use of tanning devices lacks harmonisation, as it falls within separate industries, is not well-enforced or adhered to, and the responsibility lies with national governments. Whether regulation comes in the form of bans or restrictions, matching the right interventions to fit at the country level will be key in determining its success (European Commission et al., 2016; World Health Organization, 2017).

### 2.2.2. Detection and diagnosis

- Early diagnosis of melanoma is crucial to favourable outcomes: the 5 year survival rate is estimated at 95% for stage I melanoma, thinner than 1 mm, but drops to 62% for regional lymph node spread and below 20% for metastasised tumours (Balch et al., 2009). Yet a high proportion of melanomas are still detected late, at greater thickness or lymphatic spread. Contributing factors include lack of awareness and insufficient public education (such as with older men and hard to see areas of the body), low numbers of dermatologists in rural or remote areas, lack of training, time and incentives for primary care physicians in recognising early tumours and surveying high risk patients, and administrative obstacles in the referral pathway to melanoma specialists. Guidelines for primary care are essential as there is widespread under- and overdiagnosis and little

consistency around Europe in referral and surveillance strategies. Some melanoma subtypes, such as nodular melanoma, may not display usual ABCDE clinical alarm signs and grow rapidly, and represent a large proportion of late detected and fatal melanomas (Mar et al., 2013).

- A suspicious lesion must be referred to a dermatologist experienced with melanoma. While dermoscopy helps greatly in early diagnosis of melanoma, this technique is efficient only when performed by trained experts, and dermoscopy training and equipment availability vary in Europe (Forsea et al., 2016).
- Paediatric melanoma can be a diagnostic challenge as melanomas at this age are very rare, may not meet usual ABCDE criteria and may also be challenging for pathologists to determine their malignant potential.

### 2.2.3. Staging

There are many challenges in the staging of melanoma:

- Inappropriate, incomplete removal of primary melanoma, with errors in Breslow thickness, ulceration and mitoses estimation; initial wide-excision of the primary tumour that may interfere with the subsequent SLNB procedure; inadequate detection, resection and evaluation of (sentinel) lymph nodes (Dandekar et al., 2014)
- Different use of diagnostic terms/histopathological criteria by pathologists (Patrawala et al., 2016); incomplete histopathological reports; and not using the most recent TNM classification (Niebling et al., 2013)
- Insufficient knowledge of and experience in detection and treatment of satellite or in-transit metastasis
- Locoregional staging and follow-up with ultrasound techniques requires updated scanners and specific operator expertise, which can lead to inter-observer variability in the ultrasound diagnosis of lymph node stations and varying outcomes of fine needle aspirations (Voit et al., 2011)
- Underuse or overuse of diagnostic modalities, such as PET-CT, based on local availability or non-adherence to guidelines. The rate of metastatic cases among the patient population is relatively low. Extensive use of imaging modalities for staging and follow-up of early lesions may incur high costs, false-positive findings, radiation exposure, and potential contrast media-related toxicity and allergy (Stodell et al., 2017; Holtkamp et al., 2017).

### 2.2.4. Treatment

- Melanoma is at the forefront of developments in new cancer therapies, especially for metastatic disease. The past few years have seen rapid development of innovative drugs, such as anti-CTLA4 and anti-PD1 immunotherapies, and targeted therapy with BRAF and MEK inhibitors, that have dramatically changed the prognosis of melanoma. These treatments require in-depth understanding of the biology and immune responses of melanoma by oncologists, dermatologists and other health professionals; their combinations open many new possibilities that need exploration and they bring new, complex adverse effects, the management of which will need standardisation. Thus, they put significant pressure on healthcare systems to provide the required level of expertise, logistics and funding.
- The cost of these new drugs is also a major factor in their availability. More than 5000 patients with metastatic melanoma in Europe had no access to the latest drugs, according to data from a survey carried out in 2015/16, mostly due to reimbursement issues (Kandolf Sekulovic et al., 2017).
- Various surgical procedures have developed for advanced melanoma during a time when there was no effective adjuvant therapy, and there is known to be differences in procedures and a lack of high quality evidence. With rapid progress in new treatments, long-term loco-regional control and standardised surgical techniques are now

becoming imperative (Pasquali et al., 2017).

- Surgery can also need specialist approaches for locoregional recurrences, (multiple) in-transit metastases and lesions on locations such as the face and where cosmetic issues are important. Plastic surgeons need appropriate oncology training when they perform these procedures.
- Metastatic melanoma often spreads to the brain and latest techniques to treat brain metastases may not be available.
- Overall, decision making in advanced melanoma can now be complex concerning whether to carry out procedures such as lymph node dissection, and entering patients in trials for neo-adjuvant therapy.

### 2.2.5. Screening and counselling

There is no definitive evidence that population-based screening is efficient in decreasing mortality. However, targeting high-risk groups may improve cost-effectiveness and the benefit-harm balance of screening interventions (Wu et al., 2016; Johnson et al., 2017; Hübner et al., 2017). There is increasing knowledge about genetic susceptibility of melanoma, and genetic counselling is likely to become increasingly important, not only for melanoma but also for other cancers induced by the same genetic alterations (Potrony et al., 2015). Routine genetic testing is not yet recommended, and is hampered by cost and the short supply of genetic experts, although initial counselling can be carried out by well-informed dermatologists.

### 2.2.6. Inequalities

People with melanoma in Central and Eastern Europe have up to 40% lower 5 year survival rates than those in North and West Europe. This is likely to be a result of disparities across the cancer control spectrum, including access to the latest therapies and to clinical studies for new treatments. A survey found that patients at 34 oncology centres in 29 European countries may not have access to innovative drugs such as BRAF and MEK inhibitors. In Western Europe, 70% of patients were treated with innovative medicines; however, in 41% of Eastern and Southeastern Europe less than 10% of patients had access to these same medicines (Kandolf Sekulovic et al., 2017).

### 2.2.7. Special groups and rare cancers

**Young people** – While paediatric cancer units are available in many countries, units with expertise and appropriate facilities to meet the needs of adolescents and young adults are fewer, but are also required, given that melanoma is among the more common cancers in these age groups. For example, melanoma is the third most common cancer in ages 15–39 in the USA (Weir et al., 2011) and the second most common in those aged 25–49 in the UK (where more than 900 adults under the age of 35 are now diagnosed each year with melanoma) (National Institute for Health and Care Excellence (NICE), 2015). Education for awareness of melanoma and fertility preservation are other challenges.

**Older people** – Significant numbers of patients diagnosed with melanoma are above the age of 65 and the number is expected to increase owing to ageing of the population. Older patients with melanoma are heterogeneous, with differences in the number and severity of comorbidities, functional status and patient preferences. They are more often diagnosed with aggressive prognostic features such as thicker (Breslow) melanomas, higher mitotic rate and more ulceration than younger patients (Kruijff et al., 2012; Balch et al., 2013). Older patients also receive less aggressive treatment concerning SLNB, lymph node dissection and systemic treatment. The mortality rate is higher in older patients, even within subgroups of Breslow thickness. Frailty is negatively associated with disease free survival and rate of surgical complications (Lange et al., 2011). Age related differences in pathways to diagnosis may be associated with later diagnosis or inaccurate staging, which may lead to worse prognosis.

**Rare cancers** – Several melanoma types are rare and are included in projects that are increasing epidemiological and policy knowledge in



Europe. See RARECARE ([www.rarecare.eu](http://www.rarecare.eu)), Rare Cancers Europe ([www.rarecancerseurope.org](http://www.rarecancerseurope.org)) and PaedCan (<http://paedcan.ern-net.eu>), a European Reference Network for paediatric oncology.

### 2.2.8. Survivorship and surveillance

- Given the rapid expansion of novel treatment options for metastatic melanoma with long-term results, such as immunotherapies, there is likely to be an increasing need for support for long-term side-effects, and management of melanoma as a chronic disease.
- Long-term follow-up is required for melanoma patients to detect early recurrences, new secondary melanomas, and other related cancers. But a challenge is avoiding unnecessary and costly follow-up schemes, as there is no definite consensus on optimal methods and schedules of follow-up.

### 2.2.9. Cancer registration and data availability

Cancer registration practice, coverage and quality are highly unequal across Europe. Moreover, melanoma especially in early stages, may escape cancer registration as it is diagnosed outside the oncological network by facilities with different reporting policies (Forsea, 2016). Consequently, basic epidemiological data on incidence, mortality and survival are not uniformly available for all countries. Also, only a minority of cancer registries can provide sufficient data for the calculation of parameters necessary for the assessment of outcomes and quality of care (Siesling et al., 2015).

## 3. Organisation of care

Essential requirements for the organisation of melanoma care are:

- Cancer care pathways that cover the entire patient journey
- Treatment in centres appropriate to the stage and complexity of the disease
- Timeliness of care
- Multidisciplinary team (MDT) working including core and extended groups of professionals, in dedicated melanoma centres or units
- Patient-centred approach; patient information and involvement in decisions
- Audit and quality assurance of outcomes and care processes
- Education of health professionals; policies to enrol patients in clinical trials and capacity to conduct research
- A high-quality cancer registration system that shares data among centres and countries.

These topics are outlined in the following sections, with reference to national and European resources and clinical practice guidelines, where appropriate.

### 3.1. Care pathways and timelines

- Care for melanoma patients must be organised in pathways that cover the patient's journey from their point of view rather than that of the healthcare system, and pathways must correspond to current national and European evidence-based clinical practice guidelines on diagnosis, treatment and follow-up. The European Pathway Association defines a care pathway as “a complex intervention for the mutual decision making and organisation of care processes for a well-defined group of patients during a well-defined period”. This broad definition covers terms such as clinical, critical, integrated, patient pathways that are also often used. See <http://e-p-a.org/care-pathways> and also the WHO framework on integrated people-centred health services, <http://www.who.int/servicedeliverysafety/areas/people-centred-care>.
- An example of a melanoma care pathway is from the National Institute for Health and Care Excellence (NICE) (National Institute

for Health and Care Excellence (NICE), 2018), which organises its pathway for someone suspected or diagnosed with cutaneous melanoma into a flowchart for assessment, management and follow-up, and which is designed to be used alongside a guideline that covers how healthcare services for people with skin cancer should be organised in England and Wales. NICE also has accredited guidelines for uveal melanoma (Nathan et al., 2015).

- GPs and other referrers need timely access to expert assessment of a suspicious lesion. The maximum time for an appointment with a specialist for suspected adult cancer in England and Wales is 2 weeks, for example; other Western European countries have shorter targets.
- Reasonable times to report a diagnosis of melanoma and the opportunity to start treatment are crucial to timely treatment and to the wellbeing of patients. Patients with suspected melanoma must have a diagnostic excision within 1 week and be referred to be staged within 3 weeks. However, for early stage patients who have had a radical diagnostic excision, the time taken for a sentinel node procedure is not relevant to prognosis (Nelson et al., 2017; Oude Ophuis et al., 2016).
- After a diagnosis, it must be clear to the patient which professional is responsible for each step in the treatment pathway and who is following the patient during the journey (usually called a case manager or patient navigator) (European Partnership for Action Against Cancer (EPAAC), 2018). In some countries, case managers during the main stages of treatment are cancer nurses.
- Follow-up and survivorship must also be part of the care pathway. As most melanomas in Europe are diagnosed at early stages with good survival, long-term consequences are not usual, but complications of diagnostic or therapeutic measures may occur and must be addressed with continuity and appropriate support.
- For paediatric melanoma, the ERQCC expert group recommends collaboration with adult melanoma MDTs, and that second opinions on diagnosis and treatment strategy must be sought.

### 3.2. Melanoma units/centres

- The nature of melanoma lends itself to a two-tier system of care. Early stage lesions can be managed by a local dermatology unit that does not have the MDT needed in a melanoma centre that treats all cases. It is essential that all advanced cases are seen in, or in collaboration with, a specialist melanoma centre; professionals at a centre can also be part of an extended MDT covering other institutes and networks.
- An example of a two-tier model is in England and Wales, where NICE has recommended the establishment of two types of MDT – the local hospital skin cancer MDT, which could be in a general hospital and deals with routine early stage cases; and a specialist skin cancer MDT, likely to be in a cancer centre, which has expertise in advanced cases and which runs clinical trials (National Institute for Health and Clinical Excellence (NICE), 2006).
- It is essential that the specialist melanoma centre has significant expertise from a sufficient annual number of cases and that the core MDT has members with melanoma as their only, or one of their primary, interest(s). On the basis of existing evidence, the ERQCC expert group recommends that for an institution to be considered as a melanoma centre for advanced cases it should treat sufficient melanoma patients a year, although a threshold will depend on the structure of melanoma networks in a region or country and the distribution of expertise. Such centres must have the infrastructure and expertise to treat patients with advanced locoregional disease, such as in-transit metastases and/or lymph node metastases in the head/neck, axillary, groin or popliteal region; and those with unresectable stage IIIC and IV disease. Optional modalities include electrochemotherapy, CO<sub>2</sub> laser therapy, intralesional oncolytic virus therapy and isolated limb perfusion or infusion.

- For example, in the Netherlands, organisations involved in treating advanced melanoma must have a minimum case volume of 20 new patients a year for unresectable IIIC and IV metastatic melanoma, based on safety reports from clinical trials; (SONCOS (Dutch Federation of Oncological Societies), 2017) for inguinal, iliac/obturator groin dissections and for isolated limb perfusions a minimum volume of 10 procedures a year is mandatory. In Germany, certification for skin cancer units as an organ cancer centre requires at least 40 new melanoma cases a year (German Cancer Society (DKG), 2016).

### 3.3. The MDT – advanced melanoma

Treatment strategies for all advanced melanoma patients must be decided on, planned and delivered as a result of consensus among a core MDT that comprises the most appropriate members for the particular diagnosis and stage of cancer, patient characteristics and preferences, and with input from the extended community of professionals. The heart of this decision-making process is normally a weekly or more frequent MDT meeting where all cases are discussed with the objective of balancing the recommendations of clinical guidelines with the needs of the individual melanoma patient.

To properly treat melanoma, it is essential that the core MDT comprises health professionals from the following disciplines:

- Dermatology
- Pathology
- Radiology
- Nuclear medicine
- Surgery/surgical oncology
- Medical oncology
- Radiation oncology
- Interventional radiology
- Ophthalmology (for uveal melanoma)
- Nursing.

This core MDT meets to discuss:

- All advanced cases after diagnosis and staging to decide on optimal treatment
- Patients with advanced disease to decide on further treatment and follow-up
- Patients with a recurrence during follow-up, or where changes to treatment programmes are indicated and have multidisciplinary relevance and/or planned deviations from clinical practice guidelines.

Healthcare professionals from the following disciplines must also be available whenever their expertise is required (the ‘extended’ MDT):

- Geriatric oncology
- Oncology pharmacy
- Psycho-oncology
- Paediatric oncology
- Palliative care
- Rehabilitation and survivorship.

There is also an increasing understanding of the genetic predisposition to melanoma and to treatment response so it may be necessary soon to add a clinical geneticist to the extended MDT to discuss options for genetic testing and its results with patients and their families.

### 3.4. Disciplines in the core MDT

#### 3.4.1. Dermatology

Within the melanoma care pathway, the role of dermatologists

includes:

- Early diagnosis of cutaneous melanoma – primary tumours and recurrences
- Management of intra-cutaneous neoplastic diseases (primary or metastatic)
- Dermatological follow-up
- Part of the core MDT managing advanced melanoma.

Dermatologists are likely to work in either a general hospital or local skin clinic, responsible for diagnosis, staging and excision of early stage cutaneous melanoma, or in a specialist melanoma centre as a dermatologist, participating in the MDT on all stages of melanoma, but particularly advanced stages.

#### Essential requirements

- Dermatologists at local skin clinics/hospitals must be responsible for early diagnosis of cutaneous melanoma, and must have dermoscopy equipment and training. They must perform the correct diagnostic biopsy, participate in staging the disease with the local MDT according to the latest clinical practice guidelines, and refer advanced stages to a specialist melanoma centre (Garbe et al., 2016).
- Dermatologists must be able to perform local treatments for cutaneous neoplastic disease (basic surgery with appropriate margins, topical and intralesional treatments, electrochemotherapy where available).
- Dermatologists at local skin clinics/hospitals must carry out dermatological follow-up of melanoma patients, and must have the equipment and training for total body photography and sequential digital dermoscopy.
- Dermatologists at melanoma centres must identify and screen patients at high risk of primary and recurrent melanoma and must counsel patients and relatives about primary and secondary prevention.
- Dermatologists working in specialist melanoma centres must have major interest and expertise in melanoma and must know state of the art clinical practice guidelines for the management of advanced stages, and must participate in the core MDT according to their expertise.

#### 3.4.2. Pathology

Pathologists play a vital role in the MDT in timely diagnosis, staging, prognostic/predictive assessment and clinical decision making for each patient.

#### Essential requirements

- Pathologists must be aware of the type of tissue specimens and biopsies performed on melanocytic lesions and have access to all clinical records, including patient history, clinical diagnosis and any prior or ongoing treatment.
- Pathologists must establish a correct diagnosis according to the specific tumour entities listed in the WHO classification and must supply a pathology report with a list of items for pathological staging and refinement of prognostic models according to current guidelines (synoptic check-lists or structured reports are preferred) (Gershenwald et al., 2017; Scolyer et al., 2013).
- SLNBs must be handled by the same team of pathologists involved in the reporting of primary melanomas. If this is not possible, there must be coordination among pathology teams to ensure discussion of challenging cases. National or, preferably, international protocols such as that used by the European Organisation for Research and Treatment of Cancer (EORTC)/European Association of Nuclear medicine (EANM) for SLNB must be applied (Chakera et al., 2009).
- Second opinion must be provided for all patients with complex melanocytic skin lesions of uncertain or ambiguous

histopathological diagnosis, including lesions labelled as ‘melanocytic tumour of uncertain malignant potential’ (MELTUMP). Access to the genetic information provided by molecular techniques such as FISH or aCGH may be helpful for diagnosis and/or assessing prognosis in such challenging cases.

- Second opinion is also mandatory in patients younger than 19 years old.
- Access to an accredited laboratory for molecular testing must be guaranteed, not necessarily on site. BRAF mutation testing must be carried out for unresectable stage III or IV melanoma; it is highly recommended for high-risk stage IIC and III disease; NRAS and c-kit testing is recommended for BRAF wild-type in both cases.

### 3.4.3. Radiology

Diagnostic imaging plays little role in the initial diagnosis of melanoma, although high-resolution sonography is being studied to replace excision biopsies of cutaneous tumours (Botar-Jid et al., 2016). Imaging plays a major role in staging and follow-up of melanoma and in post-treatment assessment of metastatic melanoma. The role of the radiologist is to help assess tumour disease extent, formulate prognosis, assess treatment response, and detect tumour recurrence.

#### Essential requirements

- Radiologists must know the peculiar pattern of lymphatic spread of melanoma (satellitosis, in-transit metastasis, lymph-node metastasis) and of the modality of haematogenous diffusion (including uncommon sites of spread).
- When performing/interpreting imaging studies, radiologists must be aware of patient history; knowledge is mandatory of the primary melanoma site, of SLNB localisation (if investigated), of the SLNB result, of any prior or concurrent site of metastatic involvement, and of any previous or ongoing treatment.
- Radiologists must have interaction with the patient – as many superficial tumour localisations are self-palpated, any minimal symptom or finding must be considered.
- Radiologists must have latest equipment. This includes dermatology transducers (> 15 MHz) and colour-Doppler mode for ultrasound, multidetector scanners (≥ 16 detector rows) for CT, high magnetic field scanners (≥ 1.5 T), liver-specific contrast media, and diffusion-weighted imaging mode for magnetic resonance (MR), workstations for CT and MR images processing (Catalano et al., 2010). Systems appropriate to lower the radiation dose must be employed, particularly for young patients.
- High-resolution ultrasound with Doppler assessment is mandatory to detect locoregional metastasis. Two-phase liver acquisition (arterial phase and portal phase) CT is necessary to improve both the sensitivity and specificity in assessing liver lesions. Chest scans must include the neck base while pelvic scans must encompass the inguocrural region. MR imaging, and particularly brain MR, must be performed in case of indeterminate or discrepant CT findings, or when radiation therapy is planned (Sofue et al., 2012).
- Radiologists must have expertise in performing ultrasound or CT-guided percutaneous procedures, including fine needle cytology, placement of presurgical guidewires, and aspiration of lymphoceles.
- Radiologists assessing melanoma response to treatment must be made aware of ongoing therapy (immunotherapy, targeted therapy, isolated limb perfusion, chemoperfusion, electrochemotherapy, etc.). They must be familiar with peculiar phenomena related to innovative therapy (pseudoprogression etc.) as well as with the main related complications. When evaluating the results of chemotherapy radiologists should use the RECIST 1.1 system but for immunotherapy, immune-related response criteria should be adopted (Nishino et al., 2014).

### 3.4.4. Nuclear medicine

Current nuclear medicine techniques in melanoma are  $^{18}\text{F}$  FDG PET/CT, SLNB with radiotracers, and SPECT or SPECT/CT.

There is evidence of the efficacy of  $^{18}\text{F}$  FDG PET/CT in selected clinical indications (Boellaard et al., 2015), and appropriate use criteria (AUC) have been published (Jadvar et al., 2017). Clinical situations where  $^{18}\text{F}$  FDG PET/CT presents high efficacy and has an impact on management are:

- Initial staging of high-risk or advanced disease patients (Jiménez-Requena et al., 2010). Based on the fact that  $^{18}\text{F}$  FDG PET/CT provides accurate initial staging, it has a prognostic value and is key in management and treatment planning decisions in these patients
- Treatment response evaluation.  $^{18}\text{F}$  FDG PET/CT has a strong role in determining the efficacy of treatment. The AUC score was appropriate (score 9 of 9)
- Detection of recurrent disease:  $^{18}\text{F}$  FDG PET/CT has a strong role in determining whether if disease has recurred after completion of therapy. The AUC score was appropriate (score 7 of 9). Early detection of relapse is key for management decisions
- Guiding biopsies with the information supplied by  $^{18}\text{F}$  FDG PET/CT, improving the probability of a successful extraction of diagnostic tissue.

SLNB with radiotracers is included in the standard of care;<sup>53</sup> SPECT/CT improves the efficacy of SLNB (Mucientes Rasilla et al., 2009).

The role of the nuclear medicine physician is to oversee all aspects of  $^{18}\text{F}$  FDG PET/CT and SLNB for patients who require these procedures, including indications, multidisciplinary algorithms and management protocols.

#### Essential requirements

- $^{18}\text{F}$ -FDG PET/CT, SLNB with radiotracers, SPECT/CT and radionuclide therapy must be available and must be managed by nuclear medicine physicians with the appropriate expertise.
- Nuclear medicine must be able to perform daily verification protocols and to react accordingly. Quality-assurance protocols must be in place. An option for ensuring the high quality of PET/CT scanners is provided by the European Association of Nuclear Medicine (EANM) through EARL accreditation.

### 3.4.5. Surgery

Surgery is the mainstay of the treatment of melanoma, especially in primary disease, although surgeons are involved in all stages.<sup>51</sup> All non-metastatic adult-type primary melanomas are removed (resected) when possible as part of frontline treatment; surgery alone can cure more than 80% of melanoma patients (based on incidence/mortality figures before the advent of new therapies).

The role of surgery in advanced melanoma is changing due to the introduction of immuno- and targeted therapies (van Zeijl et al., 2017). For oligometastatic disease, surgery with or without adjuvant systemic therapy can still be the treatment of choice (Lasithiotakis and Zoras, 2017); for locoregional unresectable disease (stage IIIC), surgery can be performed after downstaging with (combination) immunotherapy or BRAF and/or MEK inhibitors. For most patients with unresectable stage IIIC or IV disease, systemic therapy is the first line of treatment (Amann et al., 2017; Franklin et al., 2017).

Surgeons also have a role in resection of residual disease or solitary sites of disease progression.

#### Essential requirements

- After diagnosis of a primary non-metastatic melanoma, a therapeutic (re-)excision must be performed by a (dermato)surgeon informed about the excisional margins that have to be kept: 0.5 cm for melanoma in situ, 1–2 cm for melanoma with a Breslow



thickness  $< = 2$  mm and 2 cm for Breslow  $> 2$  mm.

- For therapeutic re-excisions and surgical staging procedures, there must be at least two surgeons with expertise in performing sentinel node procedures in locations specific to melanoma.
- Melanoma surgeons must have knowledge of and experience with the peculiar pattern of lymphatic spread of melanoma (satellitosis, in-transit metastasis, lymph node metastasis) and of the modalities available to treat these disease entities (CO<sub>2</sub> laser, electrochemotherapy, intralesional oncolytic virus therapy (e.g. T-VEC) and isolated limb perfusion or infusion).
- Surgical treatment of patients with cervical, axillary, (ilio)inguinal or popliteal lymph node disease must be performed at a melanoma centre, unless arrangements have been made between a melanoma unit and the specialist centre based on the expertise of the surgeons in the unit. At least 10 (ilio)inguinal and/or popliteal lymph node dissections must be performed annually at the unit/centre.
- Advanced surgical treatments for locoregional disease/recurrences and oligometastatic disease must be available at a melanoma centre. If isolated limb perfusions are performed at least 10 must be performed annually.
- Specialist surgeons, such as head and neck, plastic, gynaecological and rectal surgeons, must be available at the centre to operate on mucosal melanoma sites.

#### 3.4.6. Medical oncology

Systemic treatment should be considered not only for metastatic disease, but also for any non-operable local disease, as well as in the adjuvant setting. In a number of metastatic patients, long-term benefit must now be the main therapeutic objective given the availability of checkpoint blocking monoclonal antibodies targeting CTLA-4 and PD-1, targeted therapies acting on the MAPK pathway, and oncolytic viruses for intralesional therapy. Checkpoint blockade and targeted therapies are also becoming important in the adjuvant setting. Side-effect management is becoming a major concern with new therapies, especially immunotherapies. An up-to-date summary of treatment strategies is provided by international guidelines such as the ESMO Clinical Practice Guidelines on melanoma (Dummer et al., 2015).

The role of the medical oncologist is to coordinate the patient itinerary between dermatology, surgery, radiotherapy and medical oncology; deliver appropriate therapeutic agents at the appropriate stage of disease; assess tumour response and subsequent therapeutic strategies to manage side-effects and melanoma-related symptoms, pain in particular; manage palliative care with adequate supportive care; and plan clinical and imaging follow-up for patients rendered disease free.

##### Essential requirements

- Medical oncologists must coordinate the patient's itinerary between dermatology, surgery, radiotherapy and medical oncology.
- Medical oncologists must ensure proper systemic treatment decisions are made in the MDT in the loco-regional, adjuvant and metastatic settings for targeted therapies and immunotherapies, and in some cases chemotherapy.
- Tumour response assessment and subsequent therapeutic strategies must be determined by the medical oncologist in collaboration with other MDT members.
- Specific requirements must be carried out, such as cardiac workup (US and ECG) for MEK inhibitors, and rapid treatment of immune-related adverse events (irAE) according to algorithms. Medical oncologists must be involved with training the extended clinical team and educating patients in early detection and treatment of irAE.
- Medical oncologists must be trained to detect and treat pain and other metastatic symptoms according to international guidelines and must collaborate with palliative care specialists.
- In patients rendered disease free, medical oncologists must

implement a surveillance algorithm, including imaging modalities depending on the disease stage and relapse risk.

#### 3.4.7. Radiation oncology

Radiotherapy is used to treat melanoma with either curative or palliative intent, for skin, uveal, conjunctival, mucosal (nasal cavity/paranasal sinus sinonasal, anogenital) melanoma, and also metastases. As described in the NCCN (Coit et al., 2016) and ESMO guidelines (Dummer et al., 2015), radiotherapy should also be considered for local control.

Radiotherapy can be considered for inadequate resection margins of lentigo maligna melanoma, or postoperative in regional lymph node dissections (Henderson et al., 2015), and for positive margins of melanoma metastases when surgery is not adequate. Radiotherapy also has an important role in the treatment of melanoma brain metastases, by stereotactic or whole brain radiation. For uveal melanoma, radiotherapy (proton therapy and ocular brachytherapy) is the best conservative treatment giving excellent local control rates (Dendale et al., 2006; American Brachytherapy Society, 2014). For conjunctival and mucosal melanomas, adjuvant irradiation is part of the therapeutic strategy that increases local control rates.

Radiotherapy is a palliative treatment of many symptoms in melanoma patients.

It has been reported that the combination of radiotherapy and anti-PD-1 immunotherapy is well tolerated and leads to a significant higher tumour response rate within and outside the irradiated field (abscopal effect) on patients with metastatic melanoma (Aboudaram et al., 2017).

The role of the radiation oncologist is to determine and prescribe the most suitable dose of radiation to deliver in a particular case, and the method and technique by which this will be achieved.

##### Essential requirements

- Access to radiotherapy must be provided in the melanoma centre or through a formal collaborative agreement.
- Radiation oncologists participating in melanoma MDTs must have a special interest and expertise in the biology and treatment of melanoma and have knowledge of the efficacy of radiotherapy in melanoma.
- Access to radiotherapy equipment must be provided depending on the type of melanoma: 3D conformal RT, IMRT, orthovoltage radiotherapy, proton therapy, brachytherapy by iodine or ruthenium plaque, stereotactic radiotherapy.
- The radiotherapy centre must have agreed protocols for radiotherapy and concurrent chemoradiotherapy.
- Radiation oncologists must know the current use of adjuvant therapy in melanoma and must know about interactions between systemic therapy and radiotherapy.
- Radiation oncologists must know the indications and contraindications for adjuvant and definitive radiotherapy in melanoma, and inform patients about acute and late side-effects, and interventions to prevent them from happening or worsening.
- Radiation oncologists must be responsible for follow-up and management of early and late toxicities.
- Radiation oncologists, radiotherapists and medical physicists must have expertise in ocular radiotherapy or must refer patients to an ocular radiation oncologist.

#### 3.4.8. Interventional radiology

Interventional radiology plays an important role in the diagnosis of advanced melanoma by performing targeted biopsy of melanoma metastases or of unclear lesions, and for treatment of metastases in selected patients. Indeed, image-guided percutaneous core needle biopsy is crucial in the delivery of a safe and efficient melanoma service. The role of the interventional radiologist is to:

- Perform image-guided percutaneous core needle biopsy of unclear hepatic, pulmonary or bone lesions.
- Provide expertise and support for combined therapies in patients with metastatic disease with transarterial chemotherapies drug eluted beads (Venturini et al., 2012), chemoembolisation (Huppert et al., 2010), chemoperfusion, chemosaturation or radioembolisation (for the latter with the nuclear medicine physician) (Eschelman et al., 2013), or ablative therapies for liver and lung metastases (Shashank et al., 2014; de Baère et al., 2015).
- Perform appropriate minimally-invasive therapies according to the MDT's decision.

#### Essential requirements

- Biopsies must be performed in melanoma centres by an experienced interventional radiologist.
- Interventional radiologists performing image-guided biopsies for an unclear lesion must have training and experience, have access to appropriate imaging equipment and must implement the WHO Surgical Safety Checklist.
- Interventional radiologists must work with the MDT to plan the biopsy in patients who are surgical candidates to avoid the risk of tumour cell seeding, which may significantly hamper surgical resection.
- Interventional radiologists must discuss the role and propose use of local ablative techniques for treating liver, lung or bone metastases not amenable to, or combined with, surgery.

#### 3.4.9. Ophthalmology

Specialist ophthalmologists carry out diagnosis and treatment planning of uveal (eye) melanoma. In uveal oncology centres with a dedicated MDT the risk of misdiagnosis has dropped significantly and such MDTs are essential to a fully functional specialist melanoma centre or network and to coordinate care pathways at regional and national levels.

#### Essential requirements

- Uveal melanoma patients must be served by a MDT consisting of specialist ophthalmologists, radiation oncologists and ocular oncology nurses, with the addition of medical oncologists, radiologists and liver surgeons for systemic disease.
- Diagnostics must include ophthalmoscopy, fluorescent and indocyanine angiography, OCT, fundus photography and ultrasonography (B-scan and UBM). In case of unclear diagnosis, a transvitreal or transscleral fine needle aspirate biopsy must be considered. A full physical examination must be performed to exclude systemic disease. Staging must be performed according to the AJCC classification (American Joint Committee on Cancer (AJCC), 2016; Angi et al., 2017).
- Ocular oncology centres must offer radiotherapy (brachytherapy, proton beam irradiation) and surgical treatments.
- All patients must have a 6 month check-up for liver metastasis by ultrasound. Every patient treated with radiotherapy must have a regular check-up in the first 2 years for tumour control and regression. After 2 years the check-up intervals depend on regression of the tumour and complications of the radiotherapy.
- Genetic analysis for prognostication by analysis of chromosomal aberrations (monosomy 3, extra copies of chromosome 8), expression arrays to determine class I or class I and/or BAP1 mutations must only be performed after informed consent of the patient (Dogrusözm and Jager, 2017).
- In metastatic disease, whole body staging must be performed, including a physical examination, blood tests, and contrast-enhanced CT-scan or PET-CT. Imaging of the brain is only indicated if there

are symptoms. Isolated liver perfusion and liver resection can be considered if only liver metastases are present. There is no evidence that checkpoint inhibitors are effective in metastatic uveal melanoma.

#### 3.4.10. Nursing

Nurses are the professionals who spend most time caring for people with melanoma, and carry out a range of roles in the melanoma patient care pathway. The need for melanoma nursing skills is corroborated by England's NICE in its recommendation for a specialised nursing role (National Institute for Health and Care Excellence (NICE), 2015; National Institute of Health and Care Excellence (NICE), 2016).

#### Essential requirements

- Nurses must have detailed insight into each patient's experience on the stages of their disease, proposed treatment and side-effects (Wheeler, 2009; Pullen et al., 2011).
- Nurses must conduct holistic assessments to ensure safe, personalised and age-appropriate nursing care, and provide patient information and support that promotes self-efficacy throughout the patient journey. Validated instruments (e.g. distress thermometer) must be used where appropriate and in conjunction with other MDT members.
- Nursing interventions must be optimised to minimise side-effects (Thebeau et al., 2017) and to maximise treatment benefit and quality of life, in surgery (e.g. wound healing, lymphadenectomy), radiotherapy (e.g. radiation-induced skin injury), chemotherapy (e.g. neutropenia, sepsis), targeted therapies (e.g. adherence to the regimen of oral small molecules, immunotherapy) (Duncan, 2015), isolated limb perfusion, electroporation and clinical trials. Fatigue is often mentioned by patients and must be considered by nurses.
- When performing advanced nursing roles (e.g. case manager, nurse navigator, clinical nurse specialist), nurses must coordinate care with healthcare professionals within and outside the core MDT, including with nutrition, rehabilitation, psychosocial and palliative care services.

#### 3.5. Disciplines in the extended MDT

##### 3.5.1. Geriatric oncology

The MDT must have access to geriatricians with oncology experience. The role of the geriatric oncologist is to coordinate recommendations to other specialists about the need for personalised treatment for older patients with increased vulnerability to stressors.

#### Essential requirements

- Geriatric oncologists must ensure that older patients who are to undergo extensive surgery or systemic treatment are screened for frailty with a risk-assessment frailty screening tool (Hamaker et al., 2012; Decoster et al., 2015; Huisman et al., 2014) and subsequent comprehensive geriatric assessment when indicated. Whenever possible an estimation of life expectancy (e.g. ePrognosis) may help to prioritise medical interventions.
- A geriatric oncology team including geriatricians and other specialists must be available for all vulnerable patients and their evaluation must be discussed in the MDT meeting to offer personalised treatment.
- Geriatric oncologists must ensure the early integration of palliative care plans or geriatric interventions, especially for vulnerable patients.

##### 3.5.2. Oncology pharmacy

Oncology pharmacy plays a critical role in the care of melanoma patients, given the growing importance of new treatments. The role of the oncology pharmacist is to liaise with medical oncologists to discuss

pharmaceutical treatment, supervise the preparation of oncology drugs, work with nurses to manage therapy, counsel patients on their therapy, and work in preventive programmes and palliative care.

#### Essential requirements

- Oncology pharmacists must work closely with medical oncologists and nurses. They must have experience with interactions with other drugs and foods and with dose adjustments based on age, liver and kidney function, and knowledge of complementary and alternative medicines. Oncology pharmacists must comply with the European QuapoS guidelines (European Society of Oncology Pharmacy, 2014).
- Oncology pharmacists must work with medical oncologists and nurses to minimise side-effects and achieve best quality of life concerning therapy, giving advice for example on skin care, wound management, nutrition and management of adverse drug effects.
- Oncology pharmacists must provide personalised information for melanoma patients on their drug therapy to support adherence, i.e. on the use of oral drugs.
- Oncology pharmacists must cooperate with medical oncologists on clinical trials.
- Oncology drugs must be prepared in the pharmacy or designated area that meets pharmacy criteria, and dispensing must take place under the supervision of the oncology pharmacist.

#### 3.5.3. Psycho-oncology

About 30% of melanoma patients report clinically significant distress including anxiety and depression (Kasparian et al., 2009); symptoms of distress can continue into survivorship (Oliveria et al., 2013). Common reactions include excessive worry and rumination, difficulty concentrating, insomnia, increased use of alcohol and other drugs, social withdrawal and somatic complaints (Kasparian, 2013). There is strong evidence that psychological intervention can improve psychological outcomes (Boesen et al., 2005; Dieng et al., 2016).

The role of the psycho-oncologist is to:

- Ensure that psychosocial distress (National Comprehensive Cancer Network, 2003), and other psychological disorders and psychosocial needs, are identified by screening throughout the disease continuum, and are considered by the MDT
- Promote effective communication between patients, family members and healthcare professionals
- Support patients and family members to cope with multifaceted disease effects
- Participate in prevention (i.e., identify emotional and behavioural variables that interfere or facilitate preventive practices; increase motivation to protect oneself from sun exposure, etc.).

#### Essential requirements

- Patients must have access to a self-administered psychological assessment tool ('distress thermometer'). Scores below a certain level must be routinely managed by the primary care team; above that level there must be further clinical interviewing and screening for anxiety and depression, and referral to the most appropriate professional, such as a mental health physician.
- Psychosocial care must be provided at all stages of the disease and its treatment for patients and their families and must be present to ensure comprehensive cancer care.
- In melanoma, psychological intervention must include motivation to comply with treatment and prevention (sun protection); reduction of psychological distress; addressing disfigurement; impact of distress on young adults and their life choices; survivorship issues such as return to work; and dealing with treatment toxicities and limitations.

- Psychosocial interventions must be based on clinical practice guidelines or the NCCN Guidelines for Distress Management (McLoone et al., 2013).

#### 3.5.4. Paediatric oncology

Paediatric oncology literature suggests that the clinical history of melanoma in children and adolescents resembles that of adult disease (Ferrari et al., 2014). In the absence of specific guidelines on treatment for children and adolescents, their management currently has the same approach used for adults, though it is unclear whether melanoma developing at a very young age has the same biology (and the same tumour driving mutations) of adult melanoma. There is a major challenge in researching paediatric melanoma owing to its rarity.

#### Essential requirements

- Paediatric and adolescent melanoma patients must be treated in close collaboration with a specialist adult melanoma centre.
- Paediatric doctors must be part of the MDT at all times for young patients.
- The ERQCC expert group urges that all centres that treat paediatric and adolescent melanoma participate in the European Cooperative Study Group for Pediatric Rare Tumours (EXPeRT, <http://www.raretumors-children.eu>) to work towards the goal of offering new drugs to paediatric melanoma patients (Ferrari et al., 2013).

#### 3.5.5. Palliative care

Palliative care, as defined by the World Health Organization (<http://www.who.int/cancer/palliative/definition>), applies not only at end of life but throughout cancer care. There is an increasing need for palliative care throughout the disease trajectory, especially for patients with locally advanced or metastatic melanoma to manage distressing clinical complications and symptoms and to improve the quality of life of patients and their families (Temel et al., 2010; Hui et al., 2015; Quill and Abernethy, 2013).

The role of the palliative specialist is to:

- Manage specialist palliative care and make recommendations to other specialists regarding general palliative care (e.g. symptom control)
- Identify patients in need for palliative care through systematic assessment of distressing physical, psychosocial and spiritual problems
- Provide early palliative care in conjunction with cancer specific treatments, treat disease and treatment-related distressing symptoms such as pain and dyspnoea, and offer psychosocial and spiritual care
- Provide support for family members
- Provide end-of-life care and support decision making together with primary care palliative care providers (Gallais Sörözal et al., 2016).

#### Essential requirements

- There must be a palliative care team that provides expert outpatient and inpatient care.
- The palliative care team must include specialist physicians and nurses, working with social workers, chaplains, physiotherapists, occupational therapists, dieticians, pain specialists and the psycho-oncology team.
- Palliative care specialists must have knowledge of cancer and side-effects of the oncological treatments (e.g. immune-related adverse effects), manage complications of complex skin tumours, and have experience of taking care of young patients and their families.
- The palliative care unit must collaborate with community palliative care teams.
- All patients with severe symptoms or suffering, or patients with metastatic disease, irrespective of the cancer treatment plan, must

also be in the care of the palliative care team.

### 3.5.6. Rehabilitation and survivorship

Elevated levels of distress and anxiety are experienced by melanoma survivors, with fear of developing a subsequent melanoma present in almost 75% (McLoone et al., 2011). Concerns regarding the impact of the disease on children's health is also frequently reported, given familial predisposition. Lack of consistent support and information compounds stress and fears. Reassurance and optimal communication with health professionals are considered an essential element of quality care, and 64% of melanoma patients would like to receive more information from their health professionals during follow-up (Mitchell et al., 2014). Families of patients should also be part of survivorship plans.

Surveillance programmes currently vary among countries, and guidelines are mainly based on the estimated risk of recurrence. Those with early-stage melanoma may be referred to primary health care for follow-up, the cornerstone of which is clinical examination (including total body skin examination). High-risk patients usually remain within specialised care, where signs of disease are being sought more actively through more frequent visits and imaging studies. The patient's contribution to finding superficial recurrences is important, as is reducing risk from sun exposure.

Research is ongoing into the evidence base for cost-effective surveillance and the ERQCC expert group considers that health service providers must keep abreast of the latest findings.

#### Essential requirements

- Many cancer patients are living longer after their treatment, and must be well-informed about late-effects, particularly relating to surgery (lymphoedema and scarring) and immunotherapies (permanent endocrine and auto-immune issues), and recurrences and how their lives could be affected.
- Healthcare providers must adapt their guidelines on surveillance of melanoma survivors for recurrences according to evidence for (cost)-effectiveness, which is likely to change as the impact of new therapies becomes better known (Mrazek and Chao, 2014; Watts et al., 2015; Rueth et al., 2015; Damude et al., 2016).
- Patients must be educated in self-monitoring of superficial recurrences.
- Rehabilitation and survivorship must be integrated into national cancer plans and into policies concerning employment, welfare and financial services.

## 4. Other essential requirements

### 4.1. Patient involvement, access to information and transparency

- Patients must be involved in every step of the decision-making process. Their satisfaction with their care must be assessed throughout the patient care pathway. Patients must be offered relevant and understandable information to help them appreciate the process that will be followed with their treatment from the point of diagnosis. They must be supported and encouraged to engage with their health team to ask questions and obtain feedback on their treatment wherever possible. Children need to be involved in an age-appropriate manner and their parents/carers must be included in the process as appropriate.
- It is also essential that melanoma patient support organisations are involved whenever relevant throughout the patient pathway. These groups work to:
  - Improve patients' knowledge and ability to take decisions
  - Secure access to innovative therapies and improve quality of treatment
  - Support melanoma research, such as by being involved in the

better design of clinical trials

○ Advocate at national health policy level.

- Euromelanoma (euromelanoma.org) is a pan-European campaign and resource on skin cancer, prevention and early diagnosis. Melanoma Patient Network Europe is a pan-European advocacy network (melanomapatientnetwork.eu), which also has links to national melanoma patient groups in 17 European countries. The European Skin Cancer Foundation is another pan-European body (<http://www.escf-network.eu>). OcuMelUK (<https://www.ocumeluk.org>) is a UK eye cancer charity. Organisations in the USA working at global level include the Melanoma International Foundation ([melanomainternational.org](http://melanomainternational.org)), AIM at Melanoma ([aimatmelanoma.org](http://aimatmelanoma.org)), and the Melanoma Research Foundation ([melanoma.org](http://melanoma.org)).
- Conclusions on each case discussion must be made available to patients and their primary care physician. Advice on seeking second opinions must be supported.
- Cancer healthcare providers must publish on a website, or make available to patients on request, data on centre/unit performance, including:
  - Information services
  - Waiting times to first appointment
  - Pathways of cancer care
  - Numbers of patients and treatments available at the centre
  - Number of operated patients at the centre (per procedure)
  - Clinical outcomes
  - Patient experience measurements (PREMs)
  - Incidents/adverse events
  - Clinical trials.

### 4.2. Performance and quality

The ERQCC expert group recommends that melanoma centres develop:

- Performance measurement metrics/quality indicators based on the essential requirements in this paper
- Operational policies to ensure the full benefits of a coordinated clinical pathway based on published guidelines
- Accountability within the governance processes in individual institutions
- Systems to ensure safe and high-quality patient care and experience throughout the clinical pathway
- Effective data management and reporting systems
- Engagement with patients, their carers and support groups to ensure reporting of patient outcomes and experience.

To assess properly the quality of melanoma care, three categories of outcomes must be measured and collected in databases at the level of the specialist melanoma centre, regionally and/or nationally:

- Clinical outcomes
- Process outcomes
- Patient-reported outcomes (PROs).

This includes national audits where available and national cancer registration/certification.

These approaches can be developed in the context of quality management systems (QMS) depending on the health economy of an individual country. The benefits of such a system include:

- Improving processes to enhance patient safety
- Setting standards within a clinical pathway
- Ensuring appropriate resource management including workforce and financial resources



- Facilitating training opportunities
- Determining optimal outcomes with appropriate audit.

#### 4.2.1. Audit of outcomes

Data measured and collected varies among countries but it is recommended that these outcome metrics are systematically measured and collected for audit:

- % of patients discussed in the MDT prior to treatment
- % of patients discussed in the MDT after (surgical) treatment
- Proportion of patients according to clinical stage at time of diagnosis
- Proportion of patients receiving treatment with curative and palliative intent
- Volume of specific curative procedures, such as the number of patients treated with ilio-inguinal lymph node dissection, ILP, targeted therapies and immunotherapy
- Complications and toxicities
- In-hospital mortality
- 1 and 5-year overall survival rate
- Adherence to MDT recommendations.

#### 4.2.2. Multidisciplinary team performance

- All MDT decisions must be documented in an understandable manner, and must become part of patient records. Decisions taken during MDT meetings must be monitored, and deviations reported back to the MDT. It is essential that all relevant patient data, such as pathology reports, meet quality standards and are available at the time of the MDT meeting.
- The core and extended MDTs must meet at least twice a year to review the activity of the previous period based on the audited metrics, discuss changes in protocols and procedures, and improve the performance of the unit/centre. MDT performance must be quality assured both internally and by external review with demonstration of cost-effectiveness of quality improvements, and MDT guidance must be promoted nationally and written into national cancer plans.
- The ERQCC expert group strongly recommends that further attention must be given to measures of PROs, not only to agree which tools should be used, but also to use PROs more systematically as part of discussions and evaluation within the MDT.

#### 4.2.3. Accreditation

The ERQCC expert group strongly recommends participation in national or international accreditation programmes, e.g. Organisation of European Cancer Institutes (OECI) accreditation, <http://oei.selfassessment.nu/cms> (Wind et al., 2016).

#### 4.2.4. National quality examples

Most national initiatives on quality in melanoma care are recent, demonstrating that much work needs to be carried out to embed best practice, and that variation in processes is likely to be uncovered. They include the following.

- The National Institute of Health and Care Excellence (NICE) in England and Wales published a quality standard for skin cancer in 2016.<sup>80</sup> It has 7 statements that include referral for suspected melanoma within 2 weeks, lesions examined with dermoscopy, access to a skin cancer clinical nurse specialist for those with melanoma, discussion about having a SLNB for those with a IB-IIC and > 1 mm thickness tumour, and those with metastatic or unresectable disease should be offered genetic testing.
- The National Health Service in Scotland published its first melanoma quality performance indicators in 2016 (NHS Scotland, 2016). The report details targets and performance against them. There are 11 indicators, including:

- Patients with cutaneous melanoma having their diagnostic excision biopsy carried out by a skin cancer clinician
- Surgical pathology reports for melanomas undergoing diagnostic excision biopsy that contain a full set of data items
- Patients with cutaneous melanoma discussed by a multi-disciplinary team prior to definitive treatment.
- Patients with primary cutaneous melanoma undergoing clinical examination of their draining lymph node basins
- BRAF status performed in all patients with unresectable stage III or IV disease.

On the basis that there is considerable variation in the quality of cancer care in the USA, a group identified melanoma care quality indicators that hospitals can use to assess their adherence to melanoma care guidelines (Bilimoria et al., 2009). The study rejected some quality measures as impractical (such as surgical volumes owing to remote areas) but, of valid measures, notably found low adherence to indicators for lymph node evaluation.

In 2013, the first German guidelines on the diagnosis, treatment and follow-up of melanoma were published in the framework of the German guideline programme on oncology, and 12 quality indicators were developed at the same time to implement the guideline recommendations (Follmann et al., 2014). The indicators cover factors such as the margins of safety in excisions, lymph node ultrasound, SNLB, therapeutic lymphadenectomy, post-op radiation, adjuvant and BRAF therapy, and metastatic patients discussed by an MDT. Further, these indicators are now being used in Germany's cancer centre certification programme.

A general paper on standardization and evolution of quality indicators for melanoma surgery was published in 2017 (Pasquali et al., 2017), and includes quality assurance examples from the Melanoma Institute Australia, the Italian Melanoma Intergroup and the American College of Surgeons. The paper has extensive references on the development of surgical quality for melanoma.

The Dutch Melanoma Treatment Registry (DMTR) was set up in 2013 to improve the care of patients with advanced melanoma. It aims to help carry out clinical auditing, improve transparency concerning the quality of melanoma care, provide insight into real-world outcomes on effects and costs, and create a platform for research (Jochims et al., 2017).

## 5. Education and training

It is essential that each melanoma centre provides professional clinical and scientific education on the disease and that at least one person is responsible for this programme. Healthcare professionals working in melanoma must also receive training in psychosocial oncology, palliative care, rehabilitation and communication skills, tailored to patient age where relevant. Such training must also be incorporated into specialist postgraduate and undergraduate curriculums for physicians, nurses and other professionals. Nurses working in melanoma centres should undertake post-qualification education and training about providing holistic care for people being treated for melanoma throughout the patient journey.

## 6. Clinical research and population registries

- Centres treating melanomas must have clinical research programmes (either their own research or as a participant in programmes led by other centres). The research portfolio should have both interventional and non-interventional projects and include academic research. The MDT must assess all new patients for stages II–IV for eligibility to take part in academic and industry sponsored clinical trials at the centre or in research networks.
- Collaboration with European academic networks is strongly recommended – see the melanoma group of the European Organisation for Research and Treatment of Cancer (EORTC –

<http://www.eortc.org>) and the European Clinical Research Infrastructure Network (ECRIN – <http://www.ecriin.org>). In countries where clinical trials are less available, centres treating melanoma should engage with policymakers to investigate referring patients to other countries (as proposed with European Reference Networks) and should be prepared to participate in clinical trials from an organisational standpoint. Researchers at other centres should be considered as part of the extended MDT for at least annual discussion of clinical trial participation. Generally, pan-European action should be taken to increase participation of melanoma patients in clinical trials (both industry-sponsored and academic), and internet access to local clinical trial databases should be developed.

- In paediatric oncology, participation in therapy optimising studies is a standard of care in most countries. Children, adolescents, and young adults in all countries should have access to national or international multicentre studies, and accelerated access to innovative therapies if their disease progresses (Gaspar and Fern, 2016).
- Older adults are currently underrepresented in cancer clinical trials despite having a disproportionate burden of disease. Strategies to increase the participation of older adults, adolescents and young adults in clinical trials must be implemented and trials designed to take their needs into account.
- Correlative biomarker research is a crucial part of all phases of clinical studies, and requires close cooperation with biobanks such as EORTC's SPECTA programme (<http://www.eortc.org/other-research-initiatives/specta>).
- National cancer control plans must include high-quality cancer registries for melanoma to inform both clinical research and to improve the quality of care. An example is Nordcan (<http://www.dep.iarc.fr/NORDCAN>), which includes melanoma in 50 cancer types in the Nordic countries.

## 7. Conclusion

Taken together, the information presented in this paper provides a comprehensive description of the essential requirements for establishing a high-quality melanoma service. The ERQCC expert group is aware that it is not possible to propose a 'one size fits all' system for all countries, but urges that access to multidisciplinary teams and specialised treatments is guaranteed to all patients with melanoma.

## Conflict of interest

The authors declare no conflicts of interest.

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